

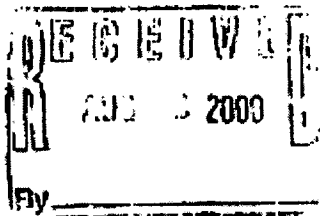
**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**20-941**

**APPROVAL LETTER**

NDA 20-941



JUL 25 2000

Avanir Pharmaceuticals  
Attention: James E. Berg  
Vice President of Clinical Affairs and Product Development  
9393 Towne Centre Drive  
Suite 200  
San Diego, CA. 92121

Dear Mr. Berg:

Please refer to your new drug application (NDA) dated December 19, 1997, received December 22, 1997, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Abreva (docosanol) Cream, 10%.

We acknowledge receipt of your submissions dated June 6, 12, July 21, and 25, 2000. Your submission of June 6, 2000 constituted a complete response to our May 30, 2000 action letter.

This new drug application provides for the use of Abreva Cream, 10% (docosanol) for cold sore/fever blister treatment.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (immediate container and carton labels submitted July 21, 2000 and amended by your July 25 fax) and must be formatted in accordance with the requirements of 21 CFR 201.66. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternately, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 20-941." Approval of this submission by FDA is not required before the labeling is used.

You are cautioned not to promote the product as an antiviral or as providing symptomatic relief of cold sores. Promotion of symptomatic benefit should be limited to the information provided in labeling, that the product shortens healing time and duration of symptoms.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We are waiving the pediatric study requirement for this action on this application.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Babette Merritt, Project Manager, at (301) 827-2222.

Sincerely,

/S/

7/25/00

Robert J. DeLap, M.D., Ph.D.  
Director Office of Drug Evaluation V  
Center for Drug Evaluation and Research

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**20-941**

**APPROVABLE LETTER**

Food and Drug Administration  
Rockville MD 20857

NDA 20-941

Avanir Pharmaceuticals  
Attention: James E. Berg  
Vice President of Clinical Affairs and Product Development  
9393 Towne Centre Drive  
Suite 200  
San Diego, CA, 92121

MAY 30 2000

Dear Mr. Berg:

Please refer to your new drug application (NDA) dated December 19, 1997, received December 22, 1997, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Abreva (docosanol) Cream, 10%.

We acknowledge receipt of your submissions dated December 22, 1998; January 8, 11, 13 and 15, February 26, March 18, 24, and 29, April 30, May 5, 14, and 24, June 25, August 3, and December 2, 1999; January 21, February 25, April 7 and May 5, 17 (two), 25, 30, 2000. Your submission of December 2, 1999 constituted a complete response to our December 22, 1998 action letter.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit revised draft labeling for the drug. The labeling should be identical in content to the enclosed labeling (immediate container and carton labels).

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Under 21 CFR 314.50(d)(5)(vi)(b), we request that you update your NDA by submitting all safety information you now have regarding your new drug. Please provide updated information as listed below. The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

1. Retabulation of all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as in your initial submission. Tables comparing adverse reactions at the time the NDA was submitted versus now will certainly facilitate review.
2. Retabulation of drop-outs with new drop-outs identified. Discuss, if appropriate.
3. Details of any significant changes or findings.

4. Summary of worldwide experience on the safety of this drug.
5. Case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.
6. English translations of any approved foreign labeling not previously submitted.
7. Information suggesting a substantial difference in the rate of occurrence of common, but less serious, adverse events.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal meeting or telephone conference with this Division to discuss what further steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, contact Kevin Darryl White, Project Manager, at (301) 827-2020.

Sincerely,

/S/

Robert J. DeLap, M.D., Ph.D.  
Director  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research

Enclosure